AMENDMENTS

In the Claims

1. (Currently Amended) A method for identifying **a ligand** ~~an agent having activity agonist activity~~ for a G protein-coupled receptor (GPCR), the method comprising:

contacting a G protein-coupled receptor (GPCR) with a candidate agent, the GPCR having a conformationally sensitive detectable probe positioned on or within a conformationally sensitive third intracellular **domain** ~~loop~~ of the GPCR **with the proviso that the probe is not positioned in a transmembrane domain**; and

detecting a detectable signal of the conformationally sensitive detectable probe;

wherein detection of a change in the detectable signal in the ~~present~~ **presence** of the candidate agent **as compared to the absence of the candidate agent** indicates the candidate agent ~~has~~ **is a ligand** ~~agonist binding activity~~ for the GPCR.

2. (Currently Amended) The method of claim 1, wherein the conformationally sensitive intracellular **domain** ~~loop~~ is a third intracellular **domain** ~~loop~~ of the GPCR and wherein the conformationally sensitive detectable probe is a detectable label attached to one or more amino acid residues within the third intracellular **domain** ~~loop~~ of the GPCR so that a conformational change in the GPCR due to agonist activity of the candidate agent causes a change in the detectable signal of the detectable label.

3. (Original) The method of claim 2, wherein the detectable label is a fluorescent probe.

4. (Original) The method of claim 2, wherein the detectable label is attached to an amino acid residue corresponding to amino acid residue at position 265 in a β2-adrenergic receptor.

5. (Withdrawn) (Currently Amended) The method of claim 1, wherein the conformationally sensitive detectable probe is a protease cleavage **site within** ~~site. within~~ the GPCR so that a conformational change in the GPCR changes the accessibility of the protease cleavage site to protease cleavage, and the detectable signal is a protease cleavage product.

6. (Withdrawn) The method of claim 5, wherein the protease cleavage product is an N-terminal fragment of the GPCR.

7. (Withdrawn) The method of claim 5, wherein the protease cleavage product is an C-terminal fragment of the GPCR.

8. (Withdrawn) (Currently Amended) The method of claim 4, wherein the detectable probe comprises two protease cleavage **sites within** ~~sties within~~ the third intracellular domain of the GPCR, the cleavage sites flanking an epitope tag, wherein a conformational change due to agonist activity changes the accessibility of the protease cleavage site to protease cleavage, and the detectable signal is a polypeptide of the epitope tag released by protease cleavage of the two cleavage sites.

9. (Original) The method of claim 1, wherein the GPCR is immobilized by attachment to a support.

10. (Original) The method of claim 9, wherein the GPCR is attached to the support by binding of an N-terminal portion to the support.

11. (Original) The method of claim 9, wherein the GPCR is attached to the support by binding of an C-terminal portion to the support.

12. (Original) The method of claim 1, wherein the GPCR is in a membrane.

13. (Withdrawn) The method of claim 5, wherein the GPCR is expressed in a eukaryotic host cell.

14. (Withdrawn) An apparatus for detecting a ligand having agonist activity for a G protein-coupled receptor, the apparatus comprising:

a G protein-coupled receptor (GPCR) with a candidate agent, the GPCR having a conformationally sensitive detectable probe positioned on or within a third intracellular loop of the GPCR; and

a immobilization phase in which the GPCR is positioned.

15. (Withdrawn) The apparatus of claim 14, wherein the conformationally sensitive detectable probe is a detectable label attached to one or more amino acid residues within the third intracellular loop of the GPCR so that a conformational change in the GPCR due to agonist activity of the candidate agent causes a change in the detectable signal of the detectable label.

16. (Withdrawn) The apparatus of claim 15, wherein the detectable label is a fluorescent probe.

17. (Withdrawn) The apparatus of claim 15, wherein the detectable label is attached to an amino acid residue corresponding to amino acid residue at position 265 in a β2-adrenergic receptor.

18. (Withdrawn) The apparatus of claim 14, wherein the conformationally sensitive detectable probe is a protease cleavage site. within the GPCR so that a conformational change in the GPCR changes the accessibility of the protease cleavage site to protease cleavage, and the detectable signal is a protease cleavage product.

19. (Withdrawn) The apparatus of claim 14, wherein the detectable probe comprises two protease cleavage sties within the third intracellular domain of the GPCR, the cleavage sites flanking an epitope tag, wherein a conformational change due to agonist activity renders the cleavage sites accessible to protease cleavage, and the detectable signal is a polypeptide of the epitope tag released by protease cleavage of the two cleavage sites.

20. (New) A method for identifying a ligand for a G protein-coupled receptor (GPCR), the method comprising:

contacting a plurality of G protein-coupled receptors (GPCRs) with a candidate agent, the GPCRs having a conformationally sensitive detectable probe positioned on or within a conformationally sensitive third intracellular domain; and

detecting a detectable signal of the conformationally sensitive detectable probe;

wherein detection of a change in the detectable signal in the presence of the candidate agent as compared to the absence of the candidate agent indicates the candidate agent is a ligand for the GPCR.

21. (New) The method of claim 20, wherein the detectable label is a fluorescent probe.

22. (New) The method of claim 20, wherein the GPCR is immobilized by attachment to a support.

23. (New) The method of claim 20, wherein the GPCR is in a membrane.